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10/699,183	11/01/2003	Robert B. More	81559/7791	1030

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FITCH EVEN TABIN AND FLANNERY
120 SOUTH LA SALLE STREET
SUITE 1600
CHICAGO, IL 60603-3406

EXAMINER	
BOWERS, NATHAN ANDREW	
ART UNIT	**PAPER NUMBER**
1744	

DATE MAILED: 02/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,183	MORE, ROBERT B.	
	Examiner	Art Unit	
	Nathan A. Bowers	1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *01 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *030404*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1) Claims 1 and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Takagi (US 20040235150).

With respect to claims 1 and 7, Takagi discloses an apparatus and method for growing a cell/tissue culture comprising providing a vessel for containing cell culture media. The bottom surface of the vessel and a rotary disc (Figure 1:24) together form a pair of approximately parallel and equidistant surfaces which define a gap. The bottom surface of the vessel and the disc form substrates that support cell tissue growth within the gap. Culture fluid circulation through the bioreactor is provided through an inlet (Figure 1:12) and an outlet (Figure 1:14). In this way, conditions that are conducive to cell tissue growth are maintained. A motor (Figure 1:40) is provided for moving the rotary disc relative to the bottom surface of the vessel so as to subject tissue growing upon and between the surfaces to physiological flow and to shear stress. This is disclosed in paragraphs [0007]-[0014] and in paragraphs [0035]-[0038].

With respect to claims 2, 3 and 8, Takagi discloses the apparatus and method in claims 1 and 7, wherein the motor is capable of rotating the disc in an oscillating manner. Paragraph [0055] indicates that the rotational direction of the disc may be changed in order to provide alternating periods of rotation in positive and negative directions.

2) Claims 1-4, 7, 8, 15 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Gemmiti (US 20050009179).

With respect to claims 1, 2, 7 and 8, Gemmiti discloses an apparatus and method for growing engineered tissue that comprises providing a vessel (Figure 1:10) for containing cell culture media. The vessel includes a top plate (Figure 1:12) and a bottom plate (Figure 1:14) form two approximately parallel and equidistant surfaces that define a gap within which cell tissue growth occurs. Cell culture media inlets (Figure 1:34) and outlets (Figure 1:36) are provided for maintaining conditions that are conducive to cell growth within the vessel. This is disclosed in paragraphs [0022]-[0026]. Paragraphs [0053]-[0055] indicate that the top plate, through a force acting upon a cap (Figure 3:18), is movable perpendicular to the cell culture and to the bottom plate. The movement of the top plate subjects the cell tissue to physiological flow and shear stresses, and may be oscillatory.

With respect to claims 3 and 4, Gemmiti discloses the apparatus in claim 2, wherein the surfaces are flat parallel plates that are aligned so as to have facing

surfaces that are substantially equidistant from each other. This is apparent from Figure 1 and from paragraphs [0022]-[0026].

With respect to claim 15, Gemmiti discloses the method in claim 8, wherein a shear stress in the range of about 10 to 1,000 dynes/cm^2 is applied. In paragraphs [0060]-[0063], Gemmiti discloses an example of operating the bioreactor in which tissue cells were subjected to shear stresses of about 15 dynes/cm^2.

With respect to claim 18, Gemmiti discloses the method in claim 7, wherein conditions are employed so as to grow a multilayered tissue material. Paragraph [0041] teaches that cells may be seeded and reseeded upon a scaffold (Figure 1:28) in order to form a multilayered tissue material.

3) Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Holl (US 20030043690).

Holl discloses a bioreactor that is inherently capable of growing engineered tissue within a vessel for containing cell-culture media. The vessel is defined by the surfaces (Figure 3:46 and Figure 3:48) of an interior cylinder (Figure 3:42) and an exterior cylinder (Figure 3:30) that are coaxially arranged. The surfaces are approximately parallel and equidistant, and define a gap in which cell growth occurs. This is disclosed in paragraph [0029]. Culture medium inlets (Figure 3:14) are provided for maintaining conditions that are conducive to cell growth with the vessel, and a motor (Figure 1:28) is provided for rotating the inner cylinder, the outer cylinder, or both cylinders, according to paragraph [0027]. Paragraph [0040] indicates that the motion of

the coaxial cylinders subjects the growing cells to physiological flow and to shear stresses.

4) Claims 1, 2, 7, 8, 13 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Sun (US 20050032200).

With respect to claims 1 and 7, Sun discloses an apparatus and method for growing engineered tissue that comprises a vessel (Figure 4:32) with a planar upper surface that is approximately parallel and approximately equidistant to the bottom surface of a disc (Figure 4:41). The two surfaces define a gap within which cell tissue growth is allowed to occur. This is disclosed in paragraphs [0008]-[0010]. The disc is attached to a motor (Figure 4:44) which causes the disc to move relative to the upper surface of the vessel in such a way that the tissue growing in between the surfaces is subjected to physiological flow and to shear stresses. Paragraph [0011] states that extraction holes are provided in the cover panel of the invention in order to facilitate the addition and extraction of solutions in an effort to maintain conditions that are conducive to cell growth.

With respect to claims 2 and 8, Sun discloses the apparatus and method in claims 1 and 7, wherein the disc moves in an oscillating motion. Paragraphs [0049]-[0051] indicate that the disc when rotating in a positive direction is capable of slowing down, stopping momentarily, and starting to rotate in a reverse, negative direction. These positive and negative rotations may be cycled in order to create an oscillating motion.

With respect to claims 13 and 17, Sun discloses the method in claim 7, wherein the cell culture media supplied in a solvent having a viscosity of about 1 centipoise. Paragraph [0028] indicates that the cultured solution has a viscosity comparable to that of water, which has a viscosity of about 1 centipoise. Furthermore, Sun teaches in paragraph [0035] that the two parallel surfaces are approximately 10 microns apart.

5) Claims 7-9 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Fofonoff (US 6281007).

Fofonoff discloses a method for growing an engineered tissue (Figure 8:502) that comprises providing facing surfaces (Figure 8:504 and Figure 8:506) within a vessel (Figure 8:525). The vessel is provided with cell culture media through an inlet port (Figure 8:522) in order to maintain conditions that are conducive to tissue growth. The surfaces move in an oscillating fashion in opposite directions relative to one another to cause the cell tissue to be subjected to physiological flow and shear stresses. This is disclosed in column 2, line 25 to column 3, line 5 and in column 10, line 60 to column 11, line 12. Fluid is allowed to enter the chamber, pressurize the chamber, and move the surfaces in outwardly horizontal directions. The surfaces are then allowed to return to their original positions. This processes is repeated in order to move the surfaces through a reciprocating motion.

6) Claims 1-4, 7, 8, 15 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Peterson (US 6121042).

With respect to claims 1 and 7, Peterson discloses an apparatus and method for growing engineered tissue that comprises providing a vessel (Figure 2:50) for containing culture media and cell tissue (Figure 2:20). Column 6, lines 28-47 indicate that the vessel is supplied with cell culture media from a reservoir (Figure 2:18) in order to maintain conditions conducive to cell growth. Column 6, line 49 to column 7, line 6 teaches that the vessel comprises a pair of approximately parallel and equidistant flat surfaces (Figure 2:52 and Figure 2:54) that define a gap within which cell growth occurs. A force generator (Figure 2:56) moves one of the surfaces relative to the other in order to subject the growing cell tissue to physiological flow and shear stresses.

With respect to claims 2 and 8, Peterson discloses that the parallel plate (Figure 2:54) that exhibits motion relative to the other parallel plate (Figure 2:52) is the end plate of a piston. Pistons are inherently characterized by back-and-forth oscillatory movements. The force generators disclosed in column 6, line 49 to column 7, line 6 would have been able to operate the piston plate according to this type of motion.

With respect to claim 11, Peterson discloses the method in claim 8, wherein the oscillating motion is carried in a generally horizontal direction. This is apparent from Figure 2 and from column 6, line 27 to column 7, line 6.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7) Claims 2, 3 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holl (US 20030043690) in view of Takagi (US 20040235150).

Holl discloses the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above, however does not expressly state that the cylinders move in an oscillating motion.

Takagi discloses a vessel for containing cell culture media that is similar to the device proposed by Holl in that a motor is provided for rotating a part of the bioreactor. Instead of rotating coaxial cylinders, Takagi teaches that the motor (Figure 1:40) is used to rotate a disc (Figure 1:24) that is capable of applying shear stresses to cells in the culturing matrix. Paragraph [0055] indicates that the rotational direction of the disc may be changed in order to provide alternating periods of rotation in positive and negative directions.

Holl and Takagi are analogous art because they are from the same field of endeavor regarding cell culturing apparatuses that are designed to impart shear stresses.

At the time of the invention, it would have been obvious to use the motor in the apparatus disclosed by Holl to rotate the inner and outer cylinders in an oscillatory manner. This would have allowed one to efficiently mix the cell culture media within the vessel, and would have provided an additional way to subject the growing cells to shear stresses. Repeatedly reversing the direction of rotation would have caused the growing cells to experience constantly changing fluidic conditions, and this would have created a more intensive conditioning environment.

8) Claims 5 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gemmiti (US 20050009179) as applied to claims 4 and 7, and further in view of Schwarz (US 5702941).

Gemmiti discloses the apparatus and method set forth in claims 4 and 7 as set forth in the 35 U.S.C. 103 rejection above, however does not expressly state that the parallel plates are gas permeable.

Schwarz discloses a bioreactor in which the walls are constructed from a gas permeable material. This is disclosed in column 4, lines 11-49. The interior volume (Figure 2:4) of the bioreactor can be altered by moving parallel surfaces (Figure 2:8) in an oscillatory manner. This is taught in column 7, lines 43-56.

Gemmiti and Schwarz are analogous art because they are from the same field of endeavor regarding bioreactors.

At the time of the invention, it would have been obvious to construct the parallel plates in the invention disclosed by Gemmiti from gas permeable materials. Schwarz teaches in column 2, lines 39-55 and column 6, lines 35-54 that assembling the components of a bioreactor out of gas permeable materials is beneficial because critical gases are allowed to directly and easily diffuse in and out of the bioreactor culturing area. If the parallel plates disclosed by Gemmiti were gas permeable, there would no longer be a need for additional exterior oxygen delivery mechanisms, which, in turn, would save considerable money and space.

9) Claims 10, 13 and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gemmiti (US 20050009179).

Gemmiti discloses the method set forth in claims 7 and 8 as set forth in the 35 U.S.C. 102 rejection above. Although Gemmiti does not expressly disclose embodiments that teach specific operational parameters, such as oscillation period, fluid viscosities, and induced strain levels, and specific design parameters such as the distance between the parallel plates, it would have been obvious to operate the bioreactor to meet the limitations disclosed in claims 10, 13 and 15-17. Varying the geometry and operation of the bioreactor to achieve the most favorable tissue culturing system is simply the optimization of result effective variables that could be pursued using routine experimentation. In the absence of new or unexpected results, it would have been obvious to ensure that the parallel plates were between 1 micron and 5 mm apart and that their period oscillation was less than 20 seconds, that the strain level was in excess of 1 with a shear stress of 10-1,000 dynes/cm^2, and that the viscosity of the culture media was at least 1 centipoise. This would guarantee that the cells in solution are subjected to an adequate conditioning environment that simulates an in vivo environment. See *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

10) Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gemmiti (US 20050009179) as applied to claim 7, and further in view of Rowley (US 20040063206).

Gemmiti discloses the method set forth in claim 7 as set forth in the 35 U.S.C. 103 rejection above. Gemmiti further discloses that the vessel is supplied with cell culture media, and that a scaffold (Figure 1:28) is provided within the vessel to facilitate tissue adhesion. Gemmiti, however, does not expressly disclose that scaffolding constituents are supplied to the bioreactor simultaneously with the cell culture media.

Rowley discloses a method of making and using a biocompatible scaffolding that promotes tissue growth. Paragraphs [0020]-[0023] teach that biologically active constituents may be attached to and implanted within the scaffolding in order to enhance cell adherence during tissue culturing procedures.

Gemmiti and Rowley are analogous art because they are from the same field of endeavor regarding tissue culturing aided by scaffolding matrixes.

At the time of the invention, it would have been obvious to the scaffolding preparation procedures disclosed by Rowley in the method disclosed by Gemmiti. The frequent addition of select constituents to the scaffolding matrix allows the scaffolding to be constantly rejuvenated and capable of facilitating cell adherence and growth. Therefore, it would have been obvious to supply the bioreactor with not only cell culture media, but also a solution containing scaffolding constituents. This would have kept the scaffolding viable and capable of supporting tissue throughout the culturing procedure.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richard Crispino can be reached on (571) 272-1226. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NAB

RICHARD CRISPINO
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1700